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510(k) SUMMARY

Submitter: Millipore Corp. (formerly Chemicon International, Inc.)
28820 Single Oak Drive
Temecula, CA 92590
Tel: (951) 676-8080
Fax: (951) 514-4482

Contact Name: Cindy Penny

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Product Name

Trade Name: ***Light Diagnostics***™ HSV 1/2 Typing DFA Kit
Common Name: Immunofluorescence Assay
Classification Name: Herpes simplex virus (21 CFR 866.3305, Product Code GQL)

Intended Use

The **Light Diagnostics™ HSV 1/2 Typing DFA Kit** is an *in vitro* diagnostic test for the qualitative detection and identification of herpes simplex virus type 1 and/or type 2 in direct specimens from patients with vesicular lesions and symptoms consistent with herpes infection and for culture confirmation by immunofluorescence. Negative results do not preclude an infection and should not be used as the sole basis for diagnosis, treatment or other management decisions. Specimens found negative on direct specimen detection should be confirmed by culture.

For In Vitro Diagnostic Use.

Predicate Device

1) Cell Culture (used to detect the absence of the HSV 1 and/or HSV 2)

Note: MRC-5 and HNF Cell Lines were used to assist clinicians in determining if the patient specimens were infected with HSV-1 and/or HSV-2 by cytopathic effect (CPE) observation. Culture grown from cells inoculated with patient specimens uses the presence or absence of CPE in the cells to identify the presence or absence of HSV in the originating patient specimen.

Device Description

Light Diagnostics™ HSV 1/2 Typing DFA Kit is a qualitative test that uses specific typing reagents and FITC filter fluorescence microscope to detect and differentiate herpes simplex viruses 1 and 2 in direct specimens from symptomatic patients with lesions and in specimens amplified by cell culture. The kit consists of HSV-1 Typing Reagent vial, HSV-2 Typing Reagent vial, two HSV Control Slides, Phosphate-Buffered Saline packet; Tween 20/Sodium Azide Solution (100X) vial, and Mounting Fluid vial. The kit utilizes specific reagents for the detection and identification of HSV-1 and HSV-2, therefore two cell spots on slides of specimens are required to identify the type of HSV. The HSV-1 Typing Reagent consists of two fluorescein-labeled monoclonal antibodies specific for HSV-1 glycoprotein C and ICP35 respectively. The HSV-2 Typing Reagent consists of two fluorescein-labeled monoclonal antibodies that specifically bind HSV-2 polypeptides. In Western blots these appear as two major bands with molecular weights of between 110-120 kD and between 78-82 kD and are consistent with the monoclonal antibodies recognizing epitopes within glycoprotein G of HSV-2. The typing reagents will bind to HSV-1 or HSV-2 infected cells fixed on microscope slides specifically. Separate cell spots on slides should be prepared for use with each reagent. Unbound reagent is removed by rinsing with phosphate-buffered saline (PBS). Illumination with ultraviolet light allows visualization of the antigen-antibody complexes by fluorescence microscopy. HSV-infected cells will exhibit apple-green fluorescence with the specific reagent while cells stain a dull red due to the presence of Evans blue in the typing reagents. The controls contained in this kit are acetone fixed slides with one well containing HSV-1 infected cells, one well containing HSV-2 infected cells, and one well containing uninfected cells to verify functioning of reagents, culture methodology and functioning of the microscope.

Technological Comparison of Methods

Comparison with Culture:

The performance characteristics of **Light Diagnostics™** HSV 1/2 Typing DFA Kit will be established by direct evaluation of clinical specimens and smear made from culture specimens using the predicate device.

An FDA cleared direct immunofluorescence test for HSV-1 and HSV-2 was used in the study to confirm with the direct specimens testing, amplified culture material, and HSV typing. The reference device is a direct immunofluorescence test intended for the detection and identification of HSV-1 and HSV-2 following amplification in cell culture or by direct examination of clinical specimens prepared by cytospin. Specimens found to be negative on direct specimen examination was tested by cell culture.

Similarities

	Light Diagnostics™ HSV 1/2 Typing DFA Kit	**Reference Device for HSV 1 and HSV 2**
Intended Use	*In vitro* diagnostic test for the qualitative detection and identification of herpes simplex virus type 1 and/or type 2 in direct specimens from patients with vesicular lesions and symptoms consistent with herpes infection and for culture confirmation by immunofluorescence. Negative results do not preclude an infection and should not be used as the sole basis for diagnosis, treatment or other management decisions. Specimens found negative on direct specimen detection should be confirmed by culture.	*In vitro* diagnostic test for direct immunofluorescence test intended for the detection and identification of herpes simplex virus type 1 (HSV-1) or herpes simplex virus type 2 (HSV-2) following amplification in cell culture or by direct examination of clinical specimens prepared by cytospin. Specimens found to be negative on direct specimen examination should be tested by cell culture.
Method	Directly labeled fluorescent antibodies specific to HSV-1 and HSV-2 to identify the presence of these viruses in patient specimens.	Directly labeled fluorescent antibodies specific to HSV-1 and HSV-2 to identify the presence of these viruses in patient specimens.
HSV 1 Antibody	The HSV-1 Typing Reagent consists of two fluorescein-labeled monoclonal antibodies specific for HSV-1 glycoprotein C and ICP35 respectively.	The primary component specific to HSV-1 will bind to the glycoprotein C and a capsid-associated protein in HSV-1 infected cells
HSV 2 Antibody	The HSV-2 Typing Reagent consists of two fluorescein-labeled monoclonal antibodies that specifically bind HSV-2 polypeptides. In Western blots these appear as two major bands with molecular weights of between 110-120 kD and between 78-82 kD and are consistent with the monoclonal antibodies recognizing epitopes within glycoprotein G of HSV-2.	The secondary component, specific for HSV-2, will bind to the glycoprotein G in HSV-2 infected cells.
Instruments required, but not provided	Fluorescence microscope with 100 watt mercury or halogen lamp, appropriate filter combination for FITC (excitation peak = 490 nm, emission peak = 520nm), 100x, 200x and 400x magnification (dry objective)	Fluorescence microscope with 100 watt mercury or halogen lamp, appropriate filter combination for FITC (excitation peak = 490 nm, emission peak = 520nm), 100x, 200x and 400x magnification (dry objective)

Differences

	Light Diagnostics™ HSV 1/2 Typing DFA Kit	**Reference Test for HSV 1 and HSV 2**
Labeling method	Two separate reagents, each of which contains FITC-labeled monoclonal antibodies directed against either HSV-1 or HSV-2. Two separate wells are necessary to detect and identify both viruses in one sample. Illumination with ultraviolet light allows visualization of the antigen-antibody complexes by fluorescence microscopy. HSV-infected cells will exhibit apple-green fluorescence with the specific reagent while cells stain a dull red due to the presence of Evans blue in the typing reagents.	One reagent contains specific monoclonal antibodies directed against HSV-1 and HSV-2 and tagged with two different fluorescent labels. This allows simultaneous visualization and identification of both HSV-1 and HSV-2-infected cells in one well. When an FITC filter set is used, HSV-1 infected cells will exhibit apple-green fluorescence and HSV-2 infected cells will exhibit yellow-gold fluorescence. The uninfected cells will stain a dull red due to the presence of Evans blue in the reagent.

Performance Data for Light Diagnostics™ HSV 1/2 Typing DFA Kit

1) Non-clinical evaluation:

The specificity of the HSV-1 and HSV-2 Typing Reagents were examined on slides prepared from HSV-1 and HSV-2 reference strains and previously typed clinical isolates after cell culture. The table below shows the results. HSV-1 and HSV-2 Typing Reagents were type-specific, showing no cross-reaction. The Typing Reagents were also tested on slides prepared from a variety of other viruses, bacteria and cell lines and showed no cross-reaction.

Cross-reactivity against common viruses, bacteria, and cell lines

Organism	**HSV-1 Reagent Result**	**HSV-2 Reagent Result**
Herpes Viruses		
Herpes simplex virus type 1; ATCC VR733/735 - Clinical isolates (8)	+	-
Herpes simplex virus type 2; ATCC VR734 - Clinical isolates(7)	-	+
Varicella zoster virus; Oka strain	-	-
Cytomegalovirus; Clinical isolate 70-35	-	-
Human herpes virus 6; strain Z-29	-	-
Epstein-Barr virus; Human Lymph. P3HR1	-	-
Other viruses		

Organism	HSV-1 Reagent Result	HSV-2 Reagent Result
Adenovirus; CDC strains V5002	-	-
Influenza A; Clinical isolate	-	-
Influenza B Clinical isolate	-	-
Mumps; CDC V5004	-	-
Parainfluenza 1; CDC V6004	-	-
Parainfluenza 2; CDC V7003	-	-
Parainfluenza 3; CDC V5003	-	-
Parainfluenza 4; ATCC strain VR-1378	-	-
Respiratory syncytial virus; CDC strain A2	-	-
Rubella; VR315 strain M-33	-	-
Bacteria		
Bordetella bronchiseptica	-	-
Bordetella pertussis	-	-
Branhamella catarrhalis	-	-
Candida albicans	-	-
Chlamydia pneumonia	-	-
Chlamydia trachomatis	-	-
Corynebacterium diptheriae	-	-
E. coli	-	-
Legionella micdadei	-	-
Legionella pneumophila	-	-
Mycobacterium tuberculosis	-	-
Mycoplasma hominis	-	-
Mycoplasma pneumoniae	-	-
Neisseria Meningitidis	-	-
Pneumocystis carinii pneumonia	-	-
Staphylococcus aureus	-*	-*
Staphylococcus epidermidis	-	-
Streptococcus pneumonia	-	-
Streptococcus pyogenes	-	-
Trichomonas vaginalis	-	-
Cell Lines		
MRC-5	-	-
A549	-	-
Vero	-	-
LLC-MK2	-	-
Hep-2	-	-

*Protein A, produced by certain bacteria, will bind the Fc portion of the monoclonal antibodies used in the Light Diagnostics™ HSV 1/2 Typing DFA Kit HSV-1 and HSV-2 reagents. Staining, however, can be differentiated by size and morphology. The presence of *Staphylococcus aureus*, a Protein A producer, will result in small (0.8μm) fluorescent spheres.

2) Clinical Evaluation:

Specimens were collected from three sites from symptomatic patients with lesions. The comparison studies were performed using Light Diagnostics™ HSV 1/2 Typing DFA Kit on direct specimens and the predicate device on specimens that grew on culture. The comparison studies were also performed using both kits on specimens that grew on culture.

The results are summarized below.

A total of 454 specimens collected from 3 clinical sites were included in this study, 258 samples were from the Eastern region of the United States and 196 from the Southeastern region of the US. The specimens include fresh vesicular fluid from herpetic lesions collected from patients with lesions and exhibiting symptoms of HSV 1 or HSV 2 infections.

Clinical samples were submitted to each laboratory in viral transport media. Cells were washed in PBS, dropped onto slides, and fixed in acetone. Slides were stained with the **Light Diagnostics™ HSV 1/2 Typing DFA Kit** reagents, and another HSV typing reagent for reference, and examined using fluorescence microscopy. All specimens were placed in MRC-5 and/or HNF standard tubes for cell culture. Slides from positive cultures were stained with the **Light Diagnostics™ HSV 1/2 Typing DFA Kit** reagents, and reference HSV typing reagent and examined using fluorescence microscopy.

Sixteen specimens were excluded from HSV-1 direct specimen analysis and 18 specimens were excluded from HSV-2 direct specimen analysis, because of insufficient numbers of cells on the direct specimen slides. The results of the remaining direct specimen slides were compared to the results of culture isolation.

Culture results were not recorded for three specimens. Analysis was performed on the remaining specimens.

Compared to culture, direct specimen testing using the **Light Diagnostics™ HSV 1/2 Typing DFA Kit** had a sensitivity of 84% (87/104) (95% Confidence Interval of 75-90%) and specificity of 99% (331/334) (95% Confidence Interval of 97% to 99%)for the detection of HSV-1; and a sensitivity of 85% (57/67) (95% Confidence Interval of 75-92%) and specificity of 99% (367/369)) (95% Confidence Interval of 98% to 99%) for the detection of HSV-2. Refer to Table 1 and Table 2.

Data from all clinical sites was combined and summarized below.

Direct specimen testing results combined from all sites

Table 1 Detection of HSV-1 in Direct Specimens using Light Diagnostics™ HSV 1/2 Typing DFA Kit vs. Culture Confirmation with HSV typing reagent.

DETECTING HSV-1		**Culture Confirmation with Predicate HSV typing reagent**			
		Positive	**Negative**	**Total**	**Comments**
Light Diagnostics™ HSV 1/2 Typing DFA Kit on Direct Specimens	**Positive**	87	3	90	Sensitivity 84% (87/104) (75-90%) 95% CI
	Negative	17	331	348	Specificity 99% (331/334) (97-99%) 95% CI
	Total	104	334	438	

Table 2
Detection of HSV-2 in Direct Specimens using Light Diagnostics™ HSV 1/2 Typing DFA Kit vs. Culture Confirmation with HSV typing reagent.

DETECTING HSV-2		**Culture Confirmation with Predicate HSV typing reagent**			
		Positive	**Negative**	**Total**	**Comments**
Light Diagnostics™ HSV 1/2 Typing DFA Kit on Direct Specimens	**Positive**	57	2	59	Sensitivity 85% (57/67) (75-92%) 95% CI
	Negative	10	367	377	Specificity 99% (367/369) (98-99%) 95% CI
	Total	67	369	436	

Culture testing using the **Light Diagnostics™ HSV 1/2 Typing DFA Kit** had a sensitivity of 100% (105/105) (95% Confidence Interval of 97-100%) and specificity of 100% (71/71) (95% Confidence Interval of 95% to 100%) for the detection of HSV-1; and a sensitivity of 100% (70/70) (95% Confidence Interval of 97-100%) and specificity of 100% (106/106))

(95% Confidence Interval of 95% to 100%) for the detection of HSV-2. Refer to Table 5 and Table 6.

Culture testing results combined from all sites

Table 3

Detection of HSV-1 using Light Diagnostics™ HSV 1/2 Typing DFA Kit vs. HSV typing reagent in culture amplified specimens.

DETECTING HSV-1		**Predicate HSV typing reagent**			
		Positive	**Negative**	**Total**	**Comments**
Light Diagnostics™ HSV 1/2 Typing DFA Kit on Culture Specimens	**Positive**	105	0	105	Sensitivity 100% (105/105) (97-100%) 95% CI
	Negative	0	71	71	Specificity 100% (71/71) (95-100%) 95% CI
	Total	105	71	176	

Table 4

Detection of HSV-2 using Light Diagnostics™ HSV 1/2 Typing DFA Kit vs. HSV typing reagent in culture amplified specimens.

DETECTING HSV-2		**Predicate HSV typing reagent**			
		Positive	**Negative**	**Total**	**Comments**
Light Diagnostics™ HSV 1/2 Typing DFA Kit on Culture Specimens	**Positive**	70	0	70	Sensitivity 100% (70/70) (95-100%) 95% CI
	Negative	0	106	106	Specificity 100% (106/106) (97-100%) 95% CI
	Total	70	106	176	

Conclusions Drawn from Evaluation:

Light Diagnostics™ HSV 1/2 Typing DFA Kit uses a standard direct immunofluorescence assay procedure for the detection of HSV type 1 and type 2 in patient specimens and in cell culture. The monoclonal antibodies used in the reagent have been characterized to ensure specificity and reliability of the product. In clinical evaluations, the performance

characteristics of the reagents were shown to be substantially equivalent to cell culture and the predicate reagent.

The characterization and clinical evaluation of the Light Diagnostics™ HSV 1/2 Typing DFA Kit demonstrates the safety and effectiveness of this product when used as intended as described in the product insert.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Cindy Penny
Regulatory Affairs Manager
Millipore Corporation
28820 Single Oak Drive
Temecula, CA 92590

APR - 1 2009

Re: K081527
Trade/Device Name: Light Diagnostics™ HSV ½ Typing DFA Kit
Regulation Number: 21 CFR 866.3305
Regulation Name: Herpes simplex virus serological reagents
Regulatory Class: Class II
Product Code: GQL
Dated: February 27, 2009
Received: March 3, 2009

Dear Ms. Penny:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): K081527

Device Name: Light Diagnostics™ HSV 1/2 Typing DFA Kit

Indication for Use:

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Prescription Use ___√___ And/Or Over the Counter Use ____.
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k): K081527